# Look-Alike/Sound-Alike (LASA) Drug Names - Review Update - Health Canada's Perspective

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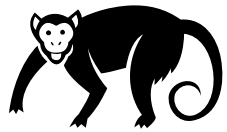
November 27, 2007

# Life of a New Drug (1)

## Research

Create/Isolate Chemicals
*(14 000 tested to get one as marketable)*
*(the average cost to develop a new medicine is 1.3 billion)*

Tissue/Culture small animals



More specific animal testing and in vitro test (eg: carcinogenicity, reproductive studies…)

Human Testing (Clinical Trial)

Special Access Programme (SAP) (emergency release)

HC approval required

All testing is done, drug company completes analysis of data, prepares a New Drug Submission (NDS)

Health Canada Review/Decision

Post Market Surveillance

Provincial Formulary Decisions

CADTH - CDR (only for NDS)

PMPRB (Price Controls)

# Life of a New Drug – Life Cycle Approach

**INDUSTRY**

Create/Isolate Chemicals
Tissue/Culture
More Specific Animal Tests

Human Testing (Clinical Trials)

Prepare New Drug Submission
Common Drug Review (CDR)

Negotiate with Provinces
Marketing and Promotion to Physicians

Updates to Product Monographs
Dear Health Care Provider Letters Actions
Product on Market or Removal

**GOVERNMENT**

New Health Canada role in drug development

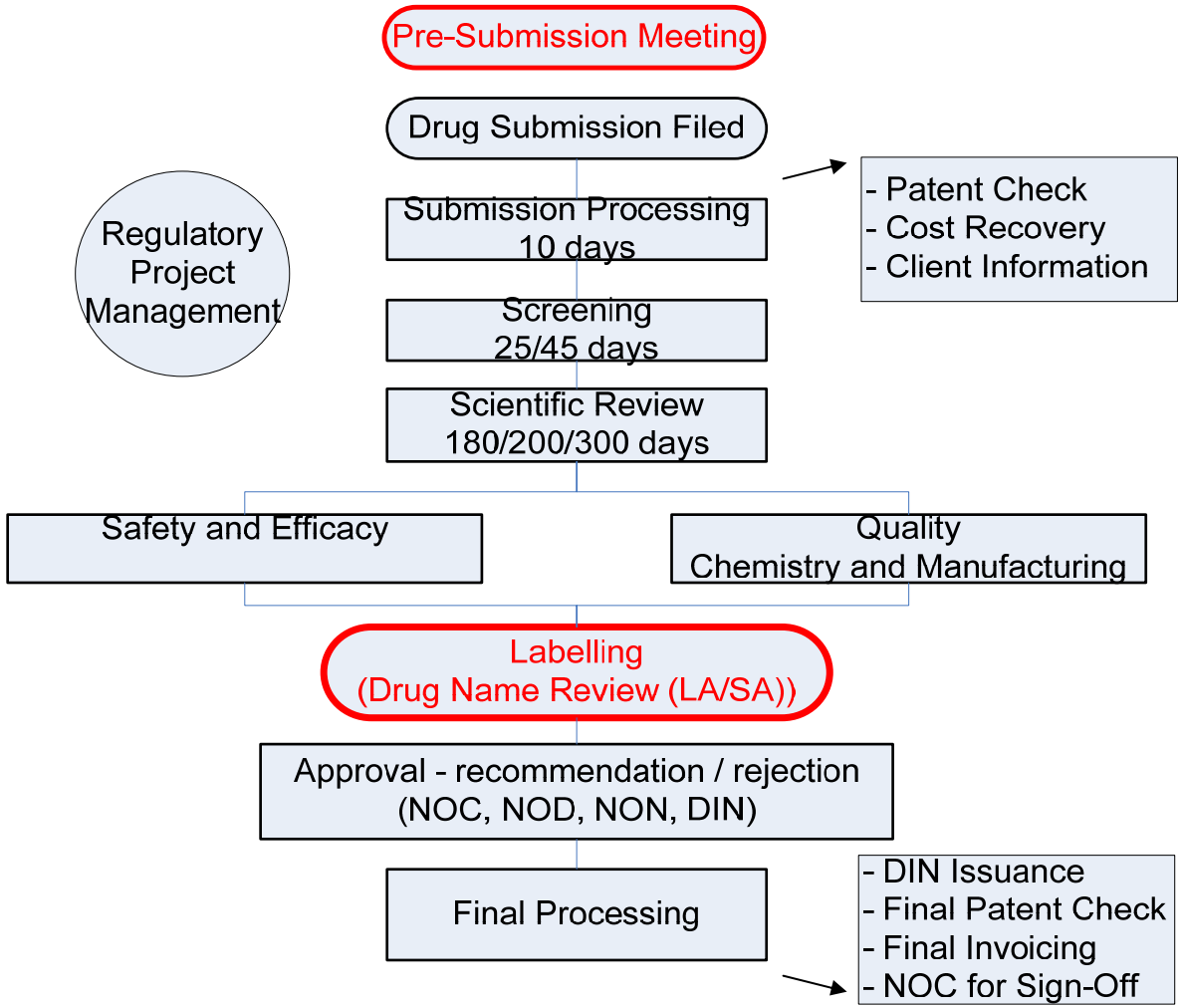
- HC Approval required
- SAP
- HC Review/Decision
- CADTH (formally CCOHTA)
- PMPRB Federal Price Control
- P/T Formulary Decisions
- Post-Market Surveillance

New Health Canada role in relation with these partners

- Post-Market Regulatory actions

Link with health professionals and consumers

# New Drug Approval Process



# Look Alike / Sound Alike (LA/SA) Drug Names

- Look-alike names have orthographic similarities
  - Confusion arises with written prescriptions
- Sound-alike names have phonetic similarities
  - Confusion arises with verbal orders

*These similarities may pose a risk to health by contributing to medical errors in prescribing, dispensing or administration of a product.*

- Name confusion accounts for one in every four medication errors[1]

[1]**B. L. Lambert et al "Similarity as a risk factor in drug-name confusion errors: the look-alike (orthographic) and sound-alike (phonetic) model". *Med Care*. 1999 Dec; 37 (12):1214-25.**

# Causes and Contributing Factors leading to Medication Errors (1)

**Human factors:**

- Stress
- Confirmation Bias
  - As Mark Twain said "*It ain't what you know what gets you in trouble it's what you know for sure that ain't so* "
- Transcription of Orders
- Prescribing
  - Similar Names
  - Incorrect  or omission of Suffixes
  - Confusing naming conventions (AF = antifungal or atrial fibrillation or advanced formula)
  - Use of Abbreviation and Trailing/Preceding Zeros on prescriptions

# Causes and Contributing Factors leading to Medication Errors (2)

**Labelling and Packaging:**

- Use of abbreviations and Trailing /preceding zeros on labels
- Expression of Strength and Total Drug Content
- Expression of Strength and Packaging Configuration
- Prominence of Information (ingredients on main panel)
- Tablet shape, color, markings
- Trade Dress - similar packaging and label color for different drugs
- Packaging Design - unmarked blister package, unreadable expiration date
- Family Trade names
- Same Trade name with different active ingredients
- Brand name extensions

# Why is HC concerned about LA/SA?

- Health Canada critically reviews scientific information in order to ensure that health products in Canada are safe, effective and of high quality
  - Safety comes into play when medical errors happen due to LA/SA drug names
  - Medication incidents are the most common single preventable cause of patient injury
  - Medication errors caused by LA/SA product names may result in adverse events
    - especially when products have different uses, and in
    - vulnerable populations - the young , the old, those with allergies, those taking other medications or those with concomitant medical conditions.
- HC's goal : reduction of the potential for confusion between the product names

# Scope of LA/SA

**Types of products**:

- Biological / Pharmaceuticals / Natural Health Products / Veterinary Products –a phased implementation

**Types of names**: Proprietary and Non-proprietary

**Pre-Market obligations:** Sponsors should undertake a review of the proposed Brand Name(s) to

- ensure that they are unlikely to cause product confusion and potential medication errors with brand name and nonproprietary names of currently marketed Canadian products.
- The results and analysis of this review should be included in the submission

**Post-Market obligations:** Sponsors should carefully consider the potential for LA/SA similarities with products that are currently marketed.

- Sponsors should monitor for occurrences of LA/SA medication errors, involving their products, that may occur “Real World” practice once a product is marketed, and
- propose mitigating risk management strategies.

## Section 9 of the Food and Drugs Act states that:

(1) No person shall label, package, treat, process, sell or advertise any drug in a manner that is false, misleading or deceptive or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.

(2) A drug that is not labelled or packaged as required by, or is labelled or packaged contrary to, the regulations shall be deemed to be labelled or packaged contrary to subsection (1)

# Who is responsible ?

**Health Care professionals**

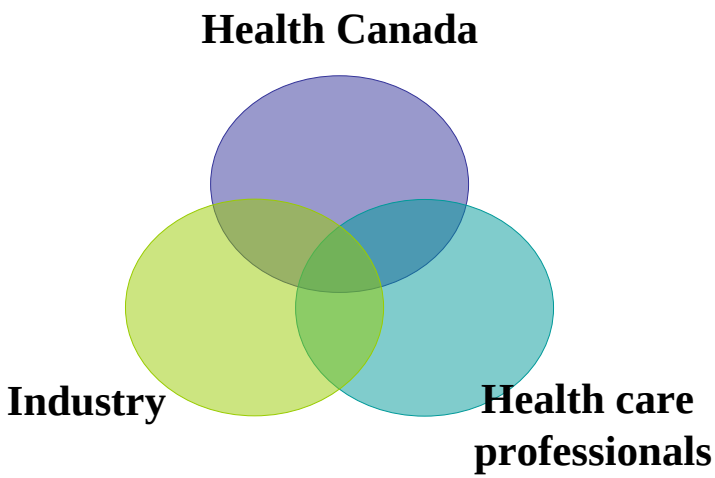
- Provide clear and well understood prescriptions
- Patient Involvement and Communication
- Reporting errors and share experiences

**Health Canada Responsibility**

- Pre-market name review
- Correcting and addressing problems quickly after approval
- Post –market surveillance
- Risk Communication and Management

**Pharmaceutical Industry**

- Clear and Concise Labeling
- Avoid Misleading or Confusing Names
- Researching the proposed name
- Choosing names that are distinctive, easily written and pronounced
- Consider errors in early development of product



# What has HC Accomplished?

- Established a Working Group
  - to review and analyze issues relating to LA/SA health product names both in the pre and post market phase and
  - to recommend an appropriate course of action
- Published LA/SA Guidance Document
  - Undertaken to review drug names prior to approval of the products
- Signed an MOU with FDA to obtain POCA Application
- Established a new Branch Medication Incidents WG
- Engaging our stakeholders (eg: CPSI, ISMP)
- Contributing to the establishment of CMIRPS (Canadian Medication Incident Reporting and prevention System)

# Factors Considered during the Drug Name Review

**In determining whether the degree of orthographic/phonetic similarity in names is problematic, the following contributing factors will be considered in the analysis as applicable :**

- the marketing status (Rx or OTC);
- therapeutic category ;
- indication(s) and directions for use ;
- the clinical setting for dispensing or use (inpatient or outpatient hospital or clinic vs. retail pharmacy for use in home);
- the packaging and labelling ;
- the strength ;
- the dosage form or routes of administration;
- the proposed dose and dosing interval;
- similar patient populations; and
- storage.

# Pre-Market Name Review Process (1)

- **All proposed proprietary names are reviewed as part of the overall pre-market review process**.
- An assessment  is done of the manufacturer's name review analysis
- An independent analysis is done using our internal databases (DSTS & DPD) -- thus only limited to the domestic market
- Multiple searches are performed using different prefixes/suffixes
- A list is created of the results
- If potential problems are flagged then a grid factor analysis is performed (see slide 15) and possibly
  - search for similar (drug/medical Reference search),
  - review of medication error literature

# Pre-Market Name Review Process (2)

- **Conclusion = Sum of all factors + Post-market factors**

- **If a potentially confusing name is identified it may be disallowed**.
  - If the sponsor has chosen to submit a prioritized list of name choices (max. of two), the subsequent name on the list will be assessed and the manufacturer may be required to change the name or
  - propose a risk assessment plan to reduce the potential for confusion between similar LA/SA products
  - HC will work with the sponsors to find an appropriate solution
  - If the sponsor did not submit a list of names and /or a drug name analysis they will be asked to provide it to us .

- **If the name is the only outstanding issue of a submission**,
  - a NOC under the proper name or ingredient name will be issued.
  - sponsors could follow-up with an Admin. NDS in order to obtain approval for a proposed brand name.

NOTE: Use of POCA (Phonetic/Orthographic Computer Analysis) – soon to be implemented

# Example of a Grid Factor Analysis

| Contributing Factors | Product A | Product B | Product C |
|---|---|---|---|
| **Use (Indication)** | Decongestant | Decongestant | Decongestant |
| **Active Ingredients** | Acetaminophen, Pseudoephedrine HCl, Phenylephrine HCl, Chlorpheniramine maleate | Acetaminophen, Pseudoephedrine HCl, Phenylephrine HCl Chlorpheniramine maleate | Acetaminophen, Pseudoephedrine HCl, Phenylephrine HCl Chlorpheniramine maleate |
| **Strengths (respectively)** | 250 mg, 30mg, 0mg, 0mg | 500mg, 0mg, 5mg, 0mg | 500mg, 0mg, 5mg, 2mg |
| **Dosage and Route of Administration** | Oral Capsules | Oral Capsules | Oral Capsules |
| **Population** | Adults and Children over 12 | Adults | Adults |
| **Dosing regimen** | 2 capsules/4-6 hours, maximum 8 caps daily | 1-2 capsules/4-6 hours, maximum 8 caps daily | 1-2 capsules/4-6 hours, maximum 8 caps daily |
| **etc…** | | | |

- Other important factors that are often considered in this analysis are
  - the **dosage form** (ie: Tablet Shape, Color, Marking),
  - the **label** (ie: color, information, declaration of ingredients, etc).

- The contributing factors can be added and/or modified as necessary.

# Phonetic/Orthographic Computer Analysis (POCA)

- Complex computer application used to detect look-alike/sound-alike similarities in health product names
  - a signal generating tool and not a decision making tool
  - to be tested and implemented in the next few months

- Application used by the U.S Food and Drug Administration (FDA).

- Health Canada has signed an agreement with the FDA to share the POCA as part of the Memorandum of Understanding between HPFB and the FDA.

# Post-Market Activities

- Contributing to the development and implementation of CMIRPS
- Coordinate with TPD/BGTD/NHPD on naming, labelling and packaging recommendations
- Partnering with healthcare providers in addressing medications incidents
- Risk communication and management

# Some Interesting Statistics

## In the United States

- Of the 25,000 medication incident reports received by the FDA each year, 12.5% of incidents are related to names[1]
- As of 2006, United States Pharmacopeia (USP) stated that 25% of all incidents reported are due to confusion over the similarity of drug names[2]

**In Canada** – similar situation

- the **Canadian Adverse Events study concludes** :
  - Adverse event rate was 7.5 per 100 hospital admissions
  - Among patients with adverse events 36.9% were preventable and death occurred in 20.8%

**[1]AJHP -Vol 58; Phillips, et al; October 1, 2001**
**[2]National Coordinating Council for Medication Error Reporting and Prevention. Council Recommendation Feb 24, 2006**

# Non-proprietary Names

## ('generic' or 'ingredient' or 'drug substance' name')

- **INN** (International Non-Proprietary Names) belongs to World Health Organization (WHO)
  - **used by HC as the primary standard of nomenclature and recommended by ICH (M5)**
    - extensive research to ensure that each INN is completely unique and will not be confused with any generic names worldwide
- **USAN** (United States Adopted Names) belongs to the USAN council
  - FDA labelling regulations require a USAN to be obtained prior to marketing
  - New revised procedures are intended to avoid inconsistencies between USAN and INN
    - previously USAN required a name only for the form of the compound to be marketed in the US , while the INN applied only for the parent molecule

# Looking Ahead

- Currently HC strongly encourages the submission of Drug Name Review by Sponsors
  - It facilitates and speeds up our own review.
  - HC may eventually consider rejecting submissions that do not include a Drug Name Review Analysis

# Current Challenges

- Balance the need to provide quick access to the drug with the possibility of producing a medication error.
- Encourage clear communication between Health care professionals and patients.
- Educate patients and consumers on the importance of reading labels and asking for the advice of health professionals .
- Evaluate error prone aspects of labelling and packaging.
- Encourage scientific research and innovation in the area of drug names assessment
  - **New methods**
  - **Determine which assessment technique is the best at predicting risk of LA/SA drug name errors.**

# Future Challenges

- Biosimilars
- Nanotechnology
- Globalization
- Environmental Concerns – re: Packaging
- Aging Population
- Communications

# Some Thoughts on the Challenges of Communicating in our Scientific Environment

- How do we  communicate scientific news, which are often complex, to a public that prefers a simple story.
  - The public needs a simple story that ensures security, certainty and predictability.

- Can we teach the public and ourselves to tolerate uncertainty and ambiguity as a normal part of life?

# Lexicon

BGTD = Biologic and Genetic Therapies Directorate
CMIRPS = Canadian Medication Incident Reporting and prevention System
CPSI = Canadian Patient Safety Institute
DPD = Drug Product Database
DSTS = Drug Submission Tracking System
FDA = Food and Drug Administration
HC = Health Canada
INN = International Non-Proprietary Names
ISMP = Institute for Safe Medication Practices
LA/SA = Look-Alike/Sound-Alike
NHPD = Natural Health Products Directorate
POCA = Phonetic/Orthographic Computer Analysis
TPD = Therapeutic Products Directorate
USAN = United States Adopted Names
USP = United States Pharmacopeia